B1 Cont This application is a nonprovisional of U.S. Application No. 60/114,408, filed 12/31/1998, now abandoned, U.S. Application No. 60/119,571 filed 2/10/1999, now abandoned, U.S. Application No. 60/139,172 filed 6/15/99, now abandoned, all of which are hereby incorporated herein by reference in their entireties.

Please amend the paragraph beginning at page 2, line 13 as follows.

This invention is directed to a β-secretase protein and in particular to a purified protein characterized by a specific activity of at least about 1.0×10^5 nM/h/μg protein in a MBP-C125sw substrate assay, which is representative β-secretase assay that uses a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (hereinafter referred to as "MBP-C125sw").

B2

Please amend the paragraph beginning at page 9, line 22 as follows.

The term "fragment," when referring to β-secretase of the invention, means a polypeptide which has an amino acid sequence which is the same as part of but not all of the amino acid sequence of full-length β-secretase polypeptide. In the context of the present invention, the full length β-secretase is generally identified as SEQ ID NO: 2, the ORF of the full-length nucleotide sequence; however, according to a discovery of the invention, the naturally occurring active form is probably one or more N-terminal truncated versions, such as amino acids 46-501, 22-501, 58-501 or 63-501; other active forms are C-terminal truncated forms ending between about amino acids 450 and 452. The numbering system used throughout is based on the numbering of the sequence SEQ ID NO: 2.

B3

Please amend the paragraph beginning at line 21 of page 63 as follows.

Recombinant proteins were generated with both the 125 C-terminus amino acids of wild-type APP sequence at the cleavage site (..Val-Lys-Met-Asp-Ala..) (SEQ ID NO: 54) (hereinafter referred to as "MBP-C125 wt") or the "Swedish" double mutation (..Val-Asn-Leu-Asp-Ala..) (SEQ ID NO: 51) (also referred to as "MBP-C125sw"). As shown in FIG. 19, cleavage of the intact MBP-fusion protein results in the generation of a truncated amino-terminal fragment, with the new SW-192 Ab-positive epitope uncovered at the carboxy terminus. This amino-terminal fragment can be recognized on Western blots with the same Ab,

B4

D